IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF GEORGIA
ATLANTA DIVISION

INTENDIS, INC. and DOW PHARMACEUTICAL SCIENCES, INC. Plaintiffs, v. RIVER'S EDGE PHARMACEUTICALS, LLC. and TERESINA HOLDINGS, LLC Defendants.	Case No. 11-cv-01634-RLV

DECLARATION OF CHRISTOPHER BOWMAN, Ph.D.

I, CHRISTOPHER BOWMAN, declare as follows:

1. I make this declaration in support of Plaintiff Intendis, Inc.'s Opening *Markman* Brief.

I. QUALIFICATIONS AND EXPERIENCE

2. I am currently the Director of the Materials Science and Engineering Program and the James and Catherine Patten Endowed Chair of Chemical and Biological Engineering at the University of Colorado at Boulder. I have been a

professor of Chemical Engineering since 1992. I am also currently a Clinical Professor of Restorative Dentistry and the Co-Director of the National Science Foundation's Industry University Cooperative Research Program (I/UCRC) for Fundamentals and Applications of Photopolymerizations.

3. I received my Bachelor of Science degree in Chemical Engineering in 1988 from Purdue University, where I graduated with Honors. I received my Doctor of Philosophy degree in Chemical Engineering from Purdue University in 1991.

4. Since the late 1980s, my research has been directed to the investigation of the formation, structure and properties of crosslinked polymeric materials. My research on crosslinked polymeric materials includes engineering polymerization reactions, synthesis of monomers and polymers, and characterization of polymeric materials. I have conducted extensive research on the properties of crosslinked polymers and their use in a variety of fields, including in pharmaceutical and biomedical applications. Throughout the course of my career, I have published articles and been an invited lecturer on photopolymerizations, polymer networks, and various other aspects of polymer science and engineering.

5. As a part of my responsibilities as a faculty member at the University of Colorado, I have taught numerous courses, including basic courses in chemistry, chemical engineering, reaction kinetics, and biology for engineers, as well as numerous advanced level classes in polymer science such as polymer chemistry, polymer engineering, and photopolymerization reactions.

6. In addition, I have taught specialty short courses or given lectures as a part of short courses taught at various venues on topics related to aspects of polymer science and engineering. These short courses and lectures have been taught at companies and at scientific meetings to industrial and academic participants as a means to provide these participants with a background and education in these advanced scientific fields. The topics of my short courses and lectures have included polymer networks, photopolymerizations, polymer science, and macromolecules and polymers of pharmaceutical interest.

7. I have been and remain a member of many professional organizations, including, for example, the American Institute of Chemical Engineers and the American Chemical Society. Most recently, I was the Organizer and Chair of the Polymer Networks 2012 Meeting, held in Jackson Hole, Wyoming. I have been a member of the National Board of Directors of the American Society for Engineering Education's Engineering Research Council, the Chair of the

Engineering Research Council Awards Committee, and have been a Director of the Materials Division of the American Institute of Chemical Engineers.

8. My complete *curriculum vitae*, which details my professional experience and includes a complete list of my honors and awards, publications, patents, invited lectures, and other relevant qualifications is attached as Exhibit A hereto.

9. The opinions set forth in this declaration concerning the nature and use of polymers in the claimed compositions are based on my personal knowledge and experience; my review of U.S. Patent No. 6,387,383 ("the '383 patent") (Lucia Ex. 1)[1] and its prosecution history; and other information and documents cited throughout this declaration.

II. SUMMARY OF OPINIONS

10. I understand that Intendis has submitted an Abbreviated New Drug Application ("ANDA") with the FDA to obtain approval to commercially manufacture, use, sell, offer for sale or import a generic copy of Intendis's DESONATE® product prior to the expiration of the '383 patent ("the ANDA Product").

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1 As used herein, "Lucia Ex. __" refers to the stated exhibit to the Declaration of Jamie Lucia, which I understand is being submitted concurrently with my declaration.

11. I understand that Dow and Intendis have asserted that River's Edge's proposed ANDA Product, if approved, would infringe claims 1, 2, 13, 18, 19, 22, 34, 37, 38, 49, and 54-59 of the '383 patent.

12. I understand that the parties disagree on the meaning of certain terms in the '383 patent and that the purpose of my declaration is to assist the Court in understanding and construing those terms.

13. I have been asked to provide my opinion as to how a person of ordinary skill in the art would have understood the term "lightly crosslinked polyacrylic acid polymer" at the time of the invention of the '383 patent.

14. In addition to the opinions expressed herein, I may provide additional opinions or testimony in response to argument presented by River's Edge in support of its opening *Markman* brief.

15. It is my opinion that a person of ordinary skill in the art would understand the term "lightly crosslinked polyacrylic acid polymer" to mean "a poly(acrylic acid) polymer crosslinked with a suitable crosslinking agent (crosslinker) at an amount less than about 5-10% (w/w)."

III. THE '383 PATENT

16. The '383 patent, entitled "Topical Low-Viscosity Gel Composition," issued on May 14, 2002, from United States Patent Application No. 09/632,508, which was filed on August 3, 2000. (Lucia Ex. 1.)

A. Specification

17. The '383 patent discloses topical low viscosity gel compositions for treating "an inflammatory skin disorder, acne, or rosacea." (Lucia Ex. 1 at ABSTRACT.) The '383 patent discloses "a composition for treating a skin disorder in a human, and a method of administering and preparing such composition." (Lucia Ex. 1 at 1:7-9.)

18. The SUMMARY OF THE INVENTION section of the '383 patent describes generally the compositions and methods of the invention. The compositions of the invention are described, for example, as "having a pH of about 3.0 to about 9.0 and a viscosity of less than about 15,000 centipoise (cP) for treating a skin disorder in a human subject." (Lucia Ex. 1 at 2:21-24.) The compositions of the invention comprise, for example, "(a) a therapeutically-effective amount of at least one compound useful for treating such disorder, (b) a pharmaceutically-acceptable polyacrylic acid polymer compatible with the

compound, (c) optionally a water miscible solvent, (d) optionally a preservative, (e) optionally an oil phase and surfactant, and (f) water." (Lucia Ex. 1 at 2:25-30.)

19. The SPECIFIC DESCRIPTION section of the '383 patent describes that a "unique aspect of the system is the use of a polymeric material that provides a gel material that has a very low viscosity but which is cosmetically elegant and aids in the administration process by providing a pourable composition that flows through a dropper tip easily." (Lucia Ex. 1 at 2:56-62.)

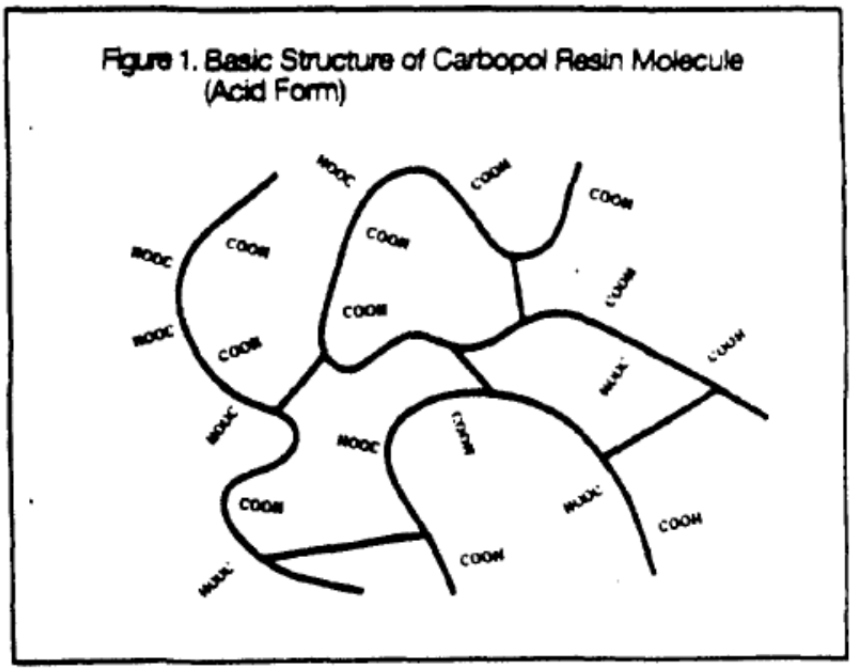
20. The SPECIFIC DESCRIPTION also describes that the claimed compositions "will include a polymeric material that will be present in an amount sufficient to bring the viscosity of the composition to a level of not more than about 15,000 cP, preferably between about 100 and about 12,000, and more preferably between about 300 and about 10,000." (Lucia Ex. 1at 4:8-13.) The '383 patent describes that, when such a polymeric material is used to achieve the desired viscosity, "the advantages of more appealing cosmetic characteristics and ease of accurate application through improved flow and pourability are achieved." (Lucia Ex. 1 at 4:18-20.)

21. The SPECIFIC DESCRIPTION describes that "polymers that have been found to be particularly useful in the composition of the present invention are lightly crosslinked polyacrylic acid polymers which are available from B.F.

Goodrich under the tradename CARBOPOL®. They are generally referred to as carbomers. The CARBOPOL polymers are hydrophilic polymers based on a polyacrylic acid structure." (Lucia Ex. 1 at 4:21-27.) Each of the CARBOPOL® products mentioned in the '383 patent specification (i.e., CARBOPOL® 910, 941, 971, 974P, 980, 981, and ETD 2050) contains a small amount of crosslinking agent and swells extensively at intermediate pH values. (*See, e.g.*, *infra* at ¶¶ 22-24.)

22. Figure 1 below from B.F. Goodrich depicts the basic structure of the unneutralized CARBOPOL® products.

Figure 1



This illustration demonstrates that this entire class of compounds is lightly crosslinked as demonstrated by the relatively small number of links between

chains. The acrylic acid repeat units are represented by the "COOH" labels. These lightly crosslinked poly(acrylic acid) polymers include all of the CARBOPOL® products mentioned in the '383 patent specification (i.e., CARBOPOL® 910, 941, 971, 974P, 980, 981, and ETD 2050).

23. The SPECIFIC DESCRIPTION describes the poly(acrylic acid) polymers of the invention as "polymers of acrylic acid crosslinked with polyalkenyl ethers or divinyl glycol." (Lucia Ex. 1 at 4:65-66.) As supported in the specification, lightly crosslinked poly(acrylic acid) polymers represent a unique and capable hydrophilic class of materials that are used here to manipulate the viscosity of gels and solutions.

24. Lightly crosslinked polymers of acrylic acid are formed by reacting acrylic acid monomers with small amounts of multi-vinyl compounds that function to form crosslinks between the polymer chains. With respect to crosslinking, the specification explains that "[e]ach primary particle can be viewed as a network structure of polymer chains interconnected by crosslinks. Without the crosslinks, the primary particle would be a collection of linear polymer chains intertwined but not chemically bonded. These linear polymers are soluble in a polar solvent, such as water. They swell in water up to 1000 times their original volume (and ten times their original diameter) to form a gel, especially when exposed to a pH

environment above about 4-6. Since the pK_a of these polymers is 6.0±0.5, the carboxylate groups on the polymer backbone ionize, resulting in repulsion between the negative particles, which adds to the swelling of the polymer." (Lucia Ex. 1 at 5:5-16.)

B. Claims

25. The '383 patent concludes with 59 claims, including 3 independent claims (claims 1, 18, 37) and 56 dependent claims. (Lucia Ex. 1 at 19:41-24:14.)

26. The asserted claims (1, 2, 13, 18, 19, 22, 34, 37, 38, 49, and 54-59) are directed to topical aqueous gel compositions, methods for treating a skin disorder in a human subject by topically administering an aqueous gel composition, and methods for preparing an aqueous gel composition.

27. Claim 1 of the '383 patent is an example of a topical aqueous gel composition claim:

> A topical aqueous gel composition having a pH of about 3 to about 9 and a viscosity of less than about 15,000 cP for treating a skin disorder in a human subject, which composition consists essentially of:
> (a) a therapeutically-effective amount of at least one compound useful for treating such disorder,
> (b) a hydrophilic pharmaceutically-acceptable, lightly crosslinked polyacrylic acid polymer compatible with the compound,
> (c) a pharmaceutically-acceptable base to adjust pH,
> (d) optionally a water miscible solvent,

(e) optionally a preservative, and
(f) water.

28. Claim 18 of the ’383 patent is an example of a method claim directed to treating a skin disorder:

> A method for treating a skin disorder in a human subject, which method comprises topically administering an aqueous gel composition having a pH of about 3 to about 9 and a viscosity of less than about 15,000 cP to an affected area of the subject’s skin having such disorder in an amount and for a period of time sufficient to improve the skin disorder, wherein the composition consists essentially of
> (a) a therapeutically-effective amount of at least one compound useful for treating such disorder,
> (b) a hydrophilic, pharmaceutically-acceptable lightly crosslinked polyacrylic acid polymer compatible with the pharmaceutical active material,
> (c) a pharmaceutically-acceptable base to adjust pH,
> (d) optionally a water miscible solvent,
> (e) optionally a preservative, and
> (f) water.

29. Claim 37 of the ’383 patent is an example of a method claim directed to preparing an aqueous gel composition:

> A method of preparing an aqueous gel composition having a viscosity of less than about 15,000 cP and a pH of about 3 to 9 useful for treating a skin disorder in a human subject, which method comprises
> (a) combining water with a therapeutically-effective amount of at least one compound useful for treating such disorder and a hydrophilic, pharmaceutically-acceptable, lightly crosslinked polyacrylic acid polymer compatible with the compound,

(b) adjusting the pH to about 3 to 9, and
(c) optionally combining a water-miscible solvent and a preservative to form the composition.

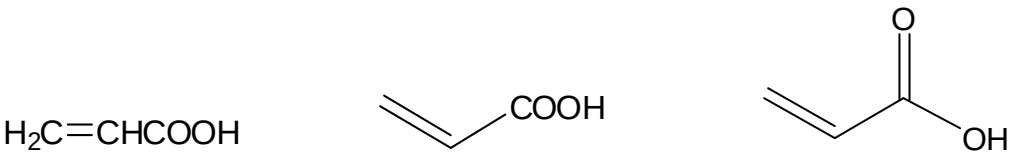
IV. BACKGROUND ON POLY(ACRYLIC ACID) POLYMERS

30. At their most basic level, crosslinked polymers are composed of polymer chains that are covalently linked together. Each of the polymer chains is comprised of individual monomeric repeat units that are coupled together to form the backbone of the polymer chain. Covalent links join the polymer chains together and are generally referred to as crosslinks because they form junctions (i.e., links) between or across two or more polymer chains. These crosslinks contribute to changes in the polymer properties, such as modulus, equilibrium degree of swelling, and viscosity.

31. The nature of crosslinked polymer behavior is dictated by the backbone forming monomer and the crosslinking agent. These "two essential monomeric materials should be present in certain proportions, although the exact proportions will vary considerably depending on the characteristics desired in the polymer." (Lucia Ex. 2 at 4:45-48.) It is well understood in polymer science that the chemical nature of the repeat unit and the extent of crosslinking control the material properties.

32. In the lightly crosslinked poly(acrylic acid) polymers that are the subject of the '383 patent, the repeat unit is formed from the acrylic acid monomer. Various representations of the acrylic acid monomer structure are illustrated below:

Figure 2



The '383 patent explains: "Since the pK_a of these polymers is 6.0±0.5, the carboxylate groups on the polymer backbone ionize, resulting in repulsion between the negative particles, which adds to the swelling of the polymer." (Lucia Ex. 1 at 5:13-16.) This acid-base neutralization reaction is unique to acid containing polymers and gives rise to pH-dependent swelling and consequently, viscosity.

33. Crosslinks between polymer chains primarily result from the inclusion of molecules that contain two or more vinyl groups that copolymerize with the acrylic acid (or other backbone forming monomer). These multi-vinyl monomers are referred to as crosslinking agents. For example, "Carbopol® resins are acrylic acid polymers crosslinked with a polyalkenyl ether." (Lucia Ex. 3 at 12.) The CARBOPOL® resins "consist essentially of a colloidally water soluble polyalkenyl

allyl ether crosslinked polymer of acrylic acid crosslinked with from 0.75 to 2.00% of a crosslinking agent." (Lucia Ex. 4 at 3:38-41; *see also* Lucia Ex. 5 at ¶ 0026; Lucia Ex. 6 at 3:24-37)

34. In the absence of any crosslinks between the polymer chains, instead of being a crosslinked polymer, the polymer material would "be a collection of linear polymer chains intertwined but not chemically bonded." (Lucia Ex. 1 at 5:7-9.)

35. In contrast, the addition of even a small amount of crosslinking agent fundamentally changes the material properties of the polymer material. For example, in considering poly(acrylic acid) polymers crosslinked by polyalkenyl ethers, "smaller amounts of the polyalkenyl ether copolymerize quite readily with carboxylic monomers and the cross-linking effect of the polyalkenyl polyether on the carboxylic monomer is so strong that as little as 0.1% by weight thereof, based on the total mixture, produces a great reduction in the water- and solvent-solubility of the polymer." (Lucia Ex. 2 at 4:53-60.) This effect is illustrative of the fact that, for lightly crosslinked poly(acrylic acid), small changes in the weight fraction of crosslinking agent have pronounced effects on the material properties.

36. Figure 3 below simultaneously illustrates the effects of crosslinking and pH on poly(acrylic acid) polymers, wherein the poly(acrylic acid) backbone

chains are illustrated by the colored lines and the crosslinks are illustrated as black rectangles:

Figure 3

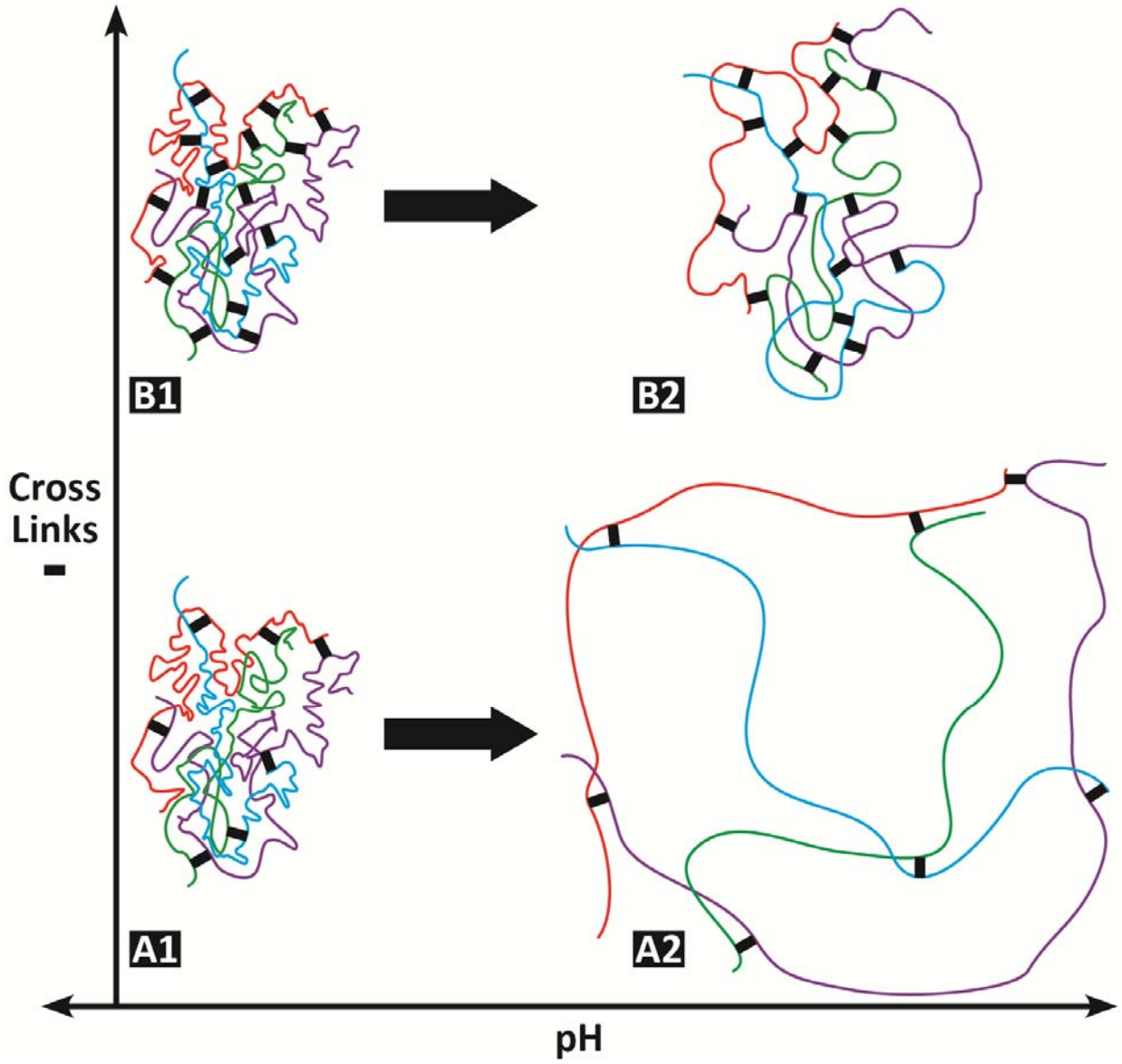
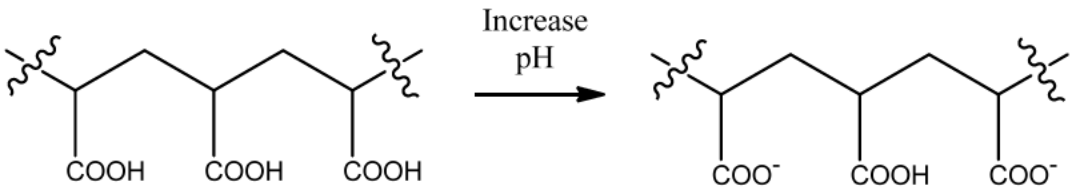


Figure 3 illustrates two different levels of crosslinking in polymers of acrylic acid: a lightly crosslinked polymer (A1 and A2) and a more densely crosslinked network

(B1 and B2). Going from left to right in the figure (i.e., A1 → A2 and B1 → B2) represents a change in the pH with the corresponding change in the degree of ionization of the carboxylic acid moieties. This effect is explained by Figure 4 below, which shows that a fraction of the backbone acrylic acid units ionize when the pH is increased:

Figure 4



As the acrylic acid units are ionized, the negative charges on the backbone repel each other and make the polymer more hydrophilic.

37. In the case of the non-crosslinked polymer, this increase in hydrophilicity leads to dissolution of the polymer, whereas, in the lightly crosslinked polymer, the system swells extensively with water as the pH increases (Figure 3, A1 → A2). By contrast, in the more densely crosslinked network, the presence of a higher level of crosslinking limits significantly the equilibrium degree of swelling (Figure 3, B1 → B2) despite the same increase in hydrophilicity.

38. Because of the corresponding changes in the polymer architecture illustrated above, the ability of these polymers to change the viscosity of solutions and gels is dependent on both pH and the extent of crosslinking. Lightly crosslinked polymers such as the CARBOPOL® resins "are hydrophilic water swellable polymers which provide . . . extremely efficient thickening with a wide range of rheological characteristics." (Lucia Ex. 7 at Section 1.1.) In contrast, the more densely crosslinked poly(acrylic acid) polymers have a higher modulus and exhibit reduced swelling in water relative to their lightly crosslinked counterparts.

V. CLAIM CONSTRUCTION

A. Claim Construction Principles

39. I understand that claim terms should be construed according to their plain and ordinary meaning, as understood by one of ordinary skill in the art at the time the inventions were made, subject to any definitions set forth in the specification. I have been asked to provide my opinion concerning the proper construction of the term "lightly crosslinked polyacrylic acid polymer." That term, as used in the '383 patent, relates to polymer science. A person of ordinary skill in the art of polymer science would have had education and training concerning the nature and use of polymers such as those in the claimed compositions. Such a person would have either a bachelor's degree in chemistry, chemical engineering,

polymer science or polymer engineering, or a related field, and at least 5-7 years of practical experience in synthetic polymers, or a doctorate degree in chemistry, chemical engineering, polymer science or polymer engineering, or a related field and at least 3-5 years of practical experience in synthetic polymers.

40. I have interpreted the claim terms of the ’383 patent consistent with the way a person of ordinary skill in the art would construe those terms.

41. In the course of determining the appropriate definition of the disputed claim terms of the ’383 patent, I have relied on my personal knowledge and experience and have reviewed the specification of the ’383 patent, the prosecution history of the ’383 patent, and the additional information and documents cited herein.

B. Construction Of “Lightly Crosslinked Polyacrylic Acid Polymer”

42. Each of the asserted claims of the ’383 patent (claims 1, 2, 13, 18, 19, 22, 34, 37, 38, 49, and 54-59) requires a “lightly crosslinked polyacrylic acid polymer.”

43. The term “lightly crosslinked polyacrylic acid polymer,” as used in the ’383 patent, and as understood by a person of ordinary skill in the art, means “a poly(acrylic acid) polymer crosslinked with a suitable crosslinking agent (crosslinker) at an amount less than about 5-10% (w/w).”

44. A person of ordinary skill in the field of polymer science would understand that a lightly crosslinked polymer, as used in the '383 patent, is generally regarded to be one in which "the concentration of crosslinking agent is much less than the concentration of monovinyl monomer." (Lucia Ex. 8 at 3177.) Thus, for a network to be considered lightly crosslinked, the concentration of the monovinyl monomer (i.e., acrylic acid in the context of '383 patent claims) should be at least 10 to 20 times the concentration of the crosslinking agent. This criteria correlates to a polymer that has no more than 5-10% crosslinking agent. Such a polymer network with less than 5-10% crosslinking agent would be lightly crosslinked.

45. In further support of this 5-10% upper limit for the range of concentration of crosslinking agent in a lightly crosslinked poly(acrylic acid) polymer, a person of ordinary skill in the art would look for guidance in the foundational patent that established this class of materials, i.e., U.S. Patent No. 2,798,053 ("the '053 patent) (Lucia Ex. 2). The '053 patent is assigned to The B.F. Goodrich Company, which introduced these polymers under the CARBOPOL® trade name (including those described and implemented in the '383 patent). (Lucia Ex. 2.)

46. Claims 2, 5, 12, 13, and 15 of the ’053 patent claim poly(acrylic acid) polymers with from 0.1 to 10% by weight of a crosslinking agent. (*See* Lucia Ex. 2 at 17:30-20:4.) One of ordinary skill in the art would use this range of crosslinking agent to identify the inclusive class of lightly crosslinked poly(acrylic acid) polymers.

47. There are numerous examples of polymers with less than 5-10% crosslinking agent that have been determined to be lightly crosslinked based on various measurements and observations:

- In Example 2 of the ’053 patent, acrylic acid polymers with 0.4, 0.7, 1.0, 1.5 and 6.0% allyl sucrose by weight were found to form highly swollen polymers with swelling indices ranging from 140 to 600. (*See* Lucia Ex. 2 at 8:55-9:38.)
- In Example 3 of the ’053 patent, 1-2% of various multivinyl crosslinking agents were used to crosslink acrylic acid and the polymers were all found to swell to more than 380 time their dry mass. (*See* Lucia Ex. 2 at 9:40-10:5.)
- In Carnali, Carbopol 940 and 941 are found to have 1450 and 3300, respectively, repeat units of acrylic acid between crosslinks. (*See* Lucia Ex. 9 at Abstract.)

48. Specific CARBOPOL® polymers, known to contain 0.75 to 2.00% crosslinking agent are described as “polyacrylic acid polymers lightly crosslinked with a polyalkenyl ether such as those commercially available from B.F. Goodrich, Cincinnati, OH under the trademarks Carbopol 934, 934P, 940, and 941.” (Lucia

Ex. 10 at 16:34-38; *see also* Lucia Ex. 11 at 4:60-5:2; Lucia Ex. 12 at 3:8-17.) Interestingly, these four specific CARBOPOL® polymers span the range of crosslinking agent content of the Carbopol family as indicated by their relative viscosities in solution. (*See, e.g.*, Lucia Ex. 7 at Section 5; Lucia Ex. 13.)

49. For these reasons, a person of ordinary skill in the art would understand the term "lightly crosslinked polyacrylic acid polymer," as used in the '383 patent, to mean "a poly(acrylic acid) polymer crosslinked with a suitable crosslinking agent (crosslinker) at an amount less than about 5-10% (w/w)."

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Dated: October 23, 2012

Christopher N. Bowman, Ph.D.